REMARKS

The Office Action mailed October 27, 2010, was reviewed and the comments of the Patent and Trademark Office were considered. In view of the above amendments and the below remarks, allowance of claims is respectfully requested.

As of the last amendment, Claims 1 and 3-34 were pending and claims 8, 27 and 30-34 were withdrawn from consideration. By this response, claims 1, 7, 8, 13 - 14, 15, 17 and 24 are amended and claims 2, 3, 6, 9 - 11 and 21 are cancelled. Support for the amendment can be found, for example, in the originally filed specification, such as paragraphs 0100 - 0105 and the originally filed claims. Applicants respectfully submit that no new matter has been added by the amendments.

Withdrawal of the rejections and allowance of all claims are respectfully requested.

35 USC § 112 REJECTIONS

Claims 1, 3-7, 9-26, 28, 29, 35 and 36 are rejected under 35 USC § 112, second paragraph.

Applicants amended the claims to remove any use of "such as", "such that" and "making it possible". Therefore, Applicants believe the amendments clarify the claimed subject matter. Applicants submit that no new matter has been added by the amendments. Furthermore, Applicants added the definition of the IG test to claim 1 as described in the specification. Applicants submit that no new matter has been added by the amendments. Additionally, claim 1 is amended to clarify the characteristics of the liquid pharmaceutical formulation.

Claims 17 - 20 are now dependent on claim 1. Claims 17 - 20 require that the [PO] further carries at least one graft of polyalkylene glycol type bonded to a glutamate or an aspartate residue. Nothing in claim 1 precludes these additional grafts on the [PO]. As such, the claim is definite.

Claim 10 is canceled without prejudice.

Withdrawal of the rejections and allowance of the claims are respectfully requested.

CLAIM REJECTIONS - 35 USC § 102

Claims 1, 16, 22, 23, 25, 26 and 36 are rejected under 35 U.S.C. 102(b) Huille et al. (U.S. Patent No. 6,630,171), hereinafter "Huille".

Claims 1, 16, 22, 23, 25, 26 and 36 are patentable over Huille. Withdrawal of the rejection and allowance of all claims are respectfully requested.

Independent claim 1, as amended, requires "wherein said [PO] is a polyamino acid formed of aspartic residues, glutamic residues, or both aspartic and glutamic residues, at least one of said residues carrying at least one tocopherol attached laterally to the chain".

Huille does not disclose use of the claimed polymer [PO] with the claimed tocopherol attached laterally to the chain. Huille does not teach use of a tocopherol.

Furthermore, independent claim 1 is amended to recite the steps of the IG test. The use of the concentration of [PO] greater than or equal to 0.9 C1 with the liquid pharmaceutical formulation of claim 1 is not found in Huille. This critical concentration 0.9 C1 at which the release time is significantly increased is now defined in amended claim 1. Huille does not disclose this limitation.

Thus, amended independent claim 1 is not anticipated by Huille. Dependent claims 16, 22, 23, 25, 26 and 36 depend from independent claim 1 and add further patentable features to the patentable features of the independent claim. Therefore, claims 1, 16, 22, 23, 25, 26 and 36 are patentable over Huille. Withdrawal of the rejection and allowance of all claims are respectfully requested.

Claim 1 is rejected under 35 U.S.C. 102(e) over Lambert (U.S. Patent No. 7,030,155), hereinafter "Lambert".

Claim 1 is patentable over Lambert. Withdrawal of the rejection and allowance of all claims are respectfully requested.

Independent claim 1, as amended, requires "wherein said [PO] is a polyamino acid formed of aspartic residues, glutamic residues, or both aspartic and glutamic residues, at least one of said residues carrying at least one tocopherol attached laterally to the chain".

Lambert does not disclose use of the claimed polymer [PO] with the claimed tocopherol *attached laterally* to the chain.

Lambert teaches that a custom surfactant can be "a vitamin E derivative comprising a peptide bonded polyglutamate attached to the ring hydroxyl and pegylated phytosterol." Lambert at C. 8, ll. 29 - 31. Lambert, therefore, teaches and discloses a surfactant including alpha-tocopherol bonded to a polyglutamate and pegylated phytosterol. The examiner alleges that the tocopherol disclosed in Lambert is equivalent to the hydrophobic group of the instant invention, the polyglutamate to the [PO] and phytosterol to the AP.

One of skill in the art would understand that the peptide disclosed in Lambert is a chain-end linking polyglutamate binding to alpha-tocopherol. For example, in C. 6, ll. 61 - 67 and in Scheme II, one molecule of PEG is bonded to one alpha-tocopherol via one succinic acid diester. Lambert therefore, teaches and discloses a polyglutamate that has only one alpha-tocopherol residue per molecule of polyglutamate. Amended claim 1 of the instant application requires polymer [PO] which can carry several tocopherols. Furthermore, these hydrophobic groups are grafted on the side chains of the polymer [PO] and not only at the chain-end. Lambert, by contrast, teaches a linear conjugate of vitamin E derivative. Thus, the composition of Lambert is different from the composition of claim 1 of the instant application. One of skill in the art would appreciate that a polyglutamate bearing a multiplicity of tocopherols on their side chains would have different structure and properties from a polyglutamate bonded to only one alpha-tocopherol.

Furthermore, independent claim 1 is amended to recite the steps of the IG test. The use of the concentration of [PO] greater than or equal to 0.9 C1 with the liquid pharmaceutical formulation of claim 1 is not found in Lambert.

Lambert does not teach the limitations of "submicronic particles of water-soluble biodegradable polymer [PO] carrying at least one tocopherol attached laterally to the chain" and "[PO] greater than or equal to 0.9.C1, where C1 is the "*induced gelling*" concentration of the particles of [PO], as measured in an induced gelling (IG) test" as required by the claims. Moreover, to obtain a release time of the active ingredient beyond 24 h after administration claim 1 requires a critical concentration of 0.9 C1 in an IG test. Lambert does not anticipate the existence of a critical concentration for which the release time is greatly increased. Additionally, Lambert does not disclose how to perform such a test in order to determine the 0.9 C1 critical concentration. The critical concentration 0.9 C1 at which the release time is significantly

increased, as well as the relation between this concentration 0.9 C1 and the *in vitro* protein-induced gelling phenomenon, are not found in Lambert.

Applicants, therefore, respectfully submits that Lambert does not anticipate amended claim 1. Withdrawal of the rejection and allowance of all claims are respectfully requested.

DOUBLE PATENTING REJECTION

Claims 1, 4, 5, 7, 12 - 16, 22, 23, 28 and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over co-pending Flamel applications (U.S. Application No. 10/580,037, U.S. Application No. 10/580,035).

Applicants note that this rejection is currently a provisional double patenting rejection as neither this application nor U.S. Application Nos. 10/580,037 or 10/580,035 currently have claims indicated as allowable by the Examiner. Applicant further notes that neither U.S. Application Nos. 10/580,037 nor 10/580,035 constitutes prior art as they have the same priority date as the instant application: November 21, 2003. Even if these applications were prior art, the claims would still be novel and non-obvious over the references. The instant claims require elements not required by these application; namely, the broadest claims require at least one tocopherol group attached laterally to the [PO] chain and require a test (IG) having the specific steps recited in claim 1.

As such, Applicants respectfully request this rejection be withdrawn. Alternatively, Applicants respectfully request that this rejection be held in abeyance at this time. Thus, at the time that either claims of this application and/or U.S. Application Nos. 10/580,037 or 10/580,035 are allowed, Applicants will revisit the necessity of filing a terminal disclaimer.

Claims 1, 7, 12 - 16, 22-26, 28 and 29 are rejected over claims 1-9 and 15-22 of the co-pending Chan (U.S. Patent No. 7,683,024).

Applicants assert that the claims are patentably distinct over U.S. Patent No. 7,683,024 ("Chan") and respectfully request the rejection be withdrawn.

First, the instant amended claims require elements not required by the cited reference; namely, the amended broadest claims require a formulation that is liquid under injection

conditions; a formulation that is liquid at physiological temperature and at physiological pH and in the presence of a physiological electrolyte in a physiological concentration, or at least one surfactant; a formulation comprising an aqueous colloidal suspension of low viscosity based on submicronic particles of water-soluble biodegradable polymer [PO] non-covalently associated with at least one active principle (AP); wherein said [PO] is a polyamino acid formed of aspartic residues, glutamic residues, or both aspartic and glutamic residues, at least one of said residues carrying at least one tocopherol group attached laterally to the chain; wherein the concentration of [PO] is greater than or equal to 0.9.C1, where C1 is the "*induced gelling*" concentration of the particles of [PO], as measured in an induced gelling (IG) test; and require a test (IG) having the specific steps recited in claim 1.

Second, Chan neither teaches nor suggests the claimed limitation of a concentration of [PO] such that [PO] ≥ 0.9.C1, where C1 is the "induced gelling" concentration of the particles of [PO], as measured in an induced gelling (IG) test. Moreover Chan does not disclose the steps of such a test.

The Examples of the current application show that this concentration (at least 0.9 C1) is critical for the increase of the release time. In example 10 of the current application, the formulation A has polymer concentration greater than 0.9 C1 whereas the formulation B has a concentration below 0.9 C1. As seen in table 6, the formulation A, which belong to the selection according to the invention, have a considerably longer release time than the formulation B, which does not belong to the selection according to the invention. The Tmax for the formulation A is about 48 hours contrary to the formulation B for which the Tmax is about 5 hours. These results show that this concentration which has been determined by using the induced gelling test according to the invention is critical for the increase of the release time.

There is no teaching in the cited prior art that suggests the skilled person to select [PO] concentrations greater than or equal to 0.9 C1 to achieve the present invention. Actually, it is to the Applicant's credit to have provided an *in vitro* test allowing to determine without undue burden the appropriate concentration of [PO] to allow a significant increase of the *in vivo* release time of an active principle, when administering the claimed formulation in a subject.

CONCLUSION

In view of the above remarks and amendments, the Applicants respectfully submit that each of the pending objections and rejections has been addressed and overcome, placing all of the claims of the present application in condition for allowance. If the Examiner believes that personal communication will expedite prosecution of this application, or should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number provided below.

Applicants believe no fee is due with this submission. If any fee is due, however, at any time during the prosecution of this application, the Director is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, under Order No. 022290.0159PTUS.

Dated: March 31, 2011

Respectfully submitted,

By: /Lacy Kolo/
Lacy Kolo
Registration No.: 55,350
PATTON BOGGS LLP
8484 Westpark Drive, 9th Floor
McLean, Virginia 22102
(703) 744-8000
(703) 744-8001 (Fax)
Attorney for Applicants